UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER OF PATENTS AND TRADEMARKS
Washington, D.C. 20231
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/881,721	06/18/2001	Yair Reisner	01/21720	7956

7590 12/17/2002

G.E. EHRLICH (1995) LTD.
c/o ANTHONY CASTORINA
SUITE 207
2001 JEFFERSON DAVIS HIGHWAY
ARLINGTON, VA 22202

EXAMINER	
BELYAVSKYI, MICHAIL A	
ART UNIT	PAPER NUMBER
1644	7

DATE MAILED: 12/17/2002

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/881,721	REISNER, YAIR	
	Examiner	Art Unit	
	Michail A Belyavskyi	1644	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for R ply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *24 April 2002* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-45* is/are pending in the application.

4a) Of the above claim(s) *22-45* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-21* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *10 September 2001* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Claims 1-45 are pending.

1. Applicant's elections of Group I , Claims 1- 21 and allogenic donor as species of a donor , sublethal conditions, as species of conditions and cells as a transplant species in Paper No. 5 are acknowledged. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)).

Upon further consideration, the prior art search has been extended to include lethal and supralethal conditions.

2. Claims 22-45 are withdrawn from further consideration by the Examiner, 37 C.F.R. § 1.142(b) as being drawn to nonelected inventions.

Claims 1-21, drawn to a method of inducing tolerance to transplant and method of transplanting a transplant, comprising a step of conditioning the recipient under sublethal, lethal or supralethal condition and wherein the transplant is a cell are under consideration in the instant application.

3. The following is a quotation of the second paragraph of 35 U.S.C. 112.

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

4. Claims 8, 18, 10 and 20 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Office Action Summary	Application No.	Applicant(s)	
	09/881,721	REISNER, YAIR	
	Examiner	Art Unit	
	Michail A Belyavskyi	1644	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *24 April 2002* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-45* is/are pending in the application.

4a) Of the above claim(s) *22-45* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-21* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *10 September 2001* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Claims 1-45 are pending.

1. Applicant's elections of Group I , Claims 1- 21 and allogenic donor as species of a donor , sublethal conditions, as species of conditions and cells as a transplant species in Paper No. 5 are acknowledged. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)).

Upon further consideration, the prior art search has been extended to include lethal and supralethal conditions.

2. Claims 22-45 are withdrawn from further consideration by the Examiner, 37 C.F.R. § 1.142(b) as being drawn to nonelected inventions.

Claims 1-21, drawn to a method of inducing tolerance to transplant and method of transplanting a transplant, comprising a step of conditioning the recipient under sublethal, lethal or supralethal condition and wherein the transplant is a cell are under consideration in the instant application.

3. The following is a quotation of the second paragraph of 35 U.S.C. 112.

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

4. Claims 8, 18, 10 and 20 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

A). Claims 8 and 18 are indefinite and ambiguous in recitation of "a characteristic associated with a myeloid phenotype". The metes and bounds of "a characteristic associated with a myeloid phenotype" are unclear and indefinite. The term " a characteristic associated with a myeloid phenotype " is not defined by the claim and the specification.

B). It is improper to recite " veto activity is enhanced per cell..." in claims 10 and 20. It is suggested that said phrase be changed to "veto activity is enhanced in each cell...".

5. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

6. Claims 1-5, 10-17 and 20-21 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Applicant is in possession of : A method of inducing tolerance to a transplant and a method of transplanting a transplant comprising culturing an HPC population under growth condition disclosed on page 49 lines 7-18 of the specification as filed, resulting in enhanced veto activity in said HPC cells that were induced to differentiate into myeloid $CD33^+$ cells.

Applicant is not in possession of : *Any* method of inducing tolerance to a transplant and *any* method of transplanting a transplant comprising culturing an HPC population under *any* growth condition suitable for enhancing veto activity in *any* HPC cells.

The specification fails to define all growth conditions suitable for enhancing veto activity in *any* HPC cells. Applicant has disclosed only a single growth condition on page 49 lines 7-18 of the specification as filed, resulting in enhanced veto activity only in $CD34^+$ HPC cells that were induced to differentiate into myeloid $CD33^+$ cells; therefore, the skilled artisan cannot envision all the contemplated growth condition and *any* HPC with enhancing veto activity broadly recited in the instant claims. Consequently, conception in either case cannot be achieved until a representative description of the structural and functional properties of the claimed invention has occurred, regardless of the complexity or simplicity of the method. Adequate written description requires more than a mere statement that it is part of the invention. See Fiers v. Revel, 25 USPQ2d 1601, 1606 (CAFC 1993).

A description of a genus of growth condition and HPC with enhancing veto activity may be achieved by means of a recitation of a representative number of growth conditions and HPC with enhancing veto activity, falling within the scope of the genus, or of a recitation of structural features common to the genus, which features constitute a substantial portion of the genus. Regents of the University of California v. Eli Lilly&Co., 119F3d 1559, 1569, 43 USPQ2d 1398, 1406 (Fed. Cir. 1997).

Vas-Cath Inc. v. Mahurkar, 19 USPQ2d 1111, makes clear that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession of the invention. The invention is, for purposes of the written description inquiry, whatever is now claimed." (See page 1117.) The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." (See Vas-Cath at page 1116.). Consequently, Applicant was not in possession of the instant claimed invention. See University of California v. Eli Lilly and Co. 43 USPQ2d 1398.

Applicant is directed to the Guidelines for the Examination of Patent Applications Under the 35 U.S.C. 112, ¶ 1 "Written Description" Requirement, Federal Register, Vol. 66, No. 4, pages 1099-1111, Friday January 5, 2001.

7. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

8. Claims 1-21 are rejected under 35 U.S.C. 103(a) as being unpatentable over US Patent 5,806,529 in view of Bachar-Lustig E et al (Blood, 1999, v 94, pp 3212-3221) , or Mobest D et al.(Biotechnology and Bioengineering, 1998, v. 60 pp. 341-347), or Vavrova et al. (Hematol.Cell Ther. 1999, v.41 pp105-112) .

The '529 Patent teaches a method of inducing tolerance to a transplant during bone marrow transplantation comprising administering HPC cells from allogenic donor (see entire document, Abstract in particular) . The '529 Patent also teaches that host patient is conditioned prior to the transplantation of hematopoietic stem cells (HPC) . Conditioning may be carried out under sublethal, lethal or supralethal conditions (see column 3, lines 51-60 in particular). The '529 Patent also teaches that donor and recipient are both humans (see Example 1 in particular). The '529 Patent also teaches that said method enable engraftment of MHC-mismatched transplants (see column 2, lines 36-42 in particular).

The '529 Patent does not teaches that said HPC cells are *ex vivo* culturing under growth conditions suitable for inducing or enhancing veto activity in at least a portion of said HPC cells and inducing differentiation of said HPC cells into $CD33^+$ myeloid phenotype cells prior to transplantation of the transplant.

Bachar-Lustig E. et al. teach that it is possible to culture HPC cells under growth conditions, suitable for inducing or enhancing veto activity of CD34+ cells by expanding *in vitro* the CD34+ cells and use them for transplantation (see entire document, abstract and page 3220 in particular). The said conditions are the same as to growth conditions disclosed in the instant specification (see Materials and Method in particular). It would be obvious to a person of ordinary skill in the art at the time the invention was made that the CD34+ HPC obtained and grown under the same conditions as disclosed in the instant specification would also be induced to differentiate into myeloid CD33+ cells with the same functional property as HPC recited in the instant claims absent a showing of unobvious property.

Mobest et al., teach *ex vivo* expansion of human CD34+ hematopoietic progenitor cells under condition suitable for inducing differentiation of said cells into $CD33^+$ myeloid phenotype cells (see entire document, Abstract in particular). Mobest et al., also teach that successful ex vivo culture and amplification of human CD34+ hematopoietic progenitor cells that would differntiate into $CD33^+$ myeloid phenotype cells offers the possibility of additional graft manipulation steps, e.g. depletion or elimination of contaminating tumor cells in Autologous grafts, amplification of bone marrow-repopulating hematopoietic cells, generation of immune effector cells, or genetic manipulation of stem cells (see page 341 in particular). The growth condition taught by Mobest et al. are the same as to growth conditions disclosed in the instant specification (see Materials and Method in particular). It would be obvious to a person of ordinary skill in the art at the time the invention was made that the CD34+ HPC obtained and grown under the same conditions as disclosed in the instant specification would also be induced to differentiate into myeloid CD33+ cells with the same functional property as HPC recited in the instant claims absent a showing of unobvious property.

Vavrova et al. teach a method of *ex vivo* expansion and differentiation of human HPC cells under growth conditions suitable for inducing or enhancing veto activity in at least a portion of said HPC cells and inducing differentiation of said HPC cells into $CD33^+$ myeloid phenotype cells (see entire document, Abstract and page 106 in particular). Vavrova et al. teach that *ex vivo* expansion of HPC would benefit studies including accelerated engraftment, reduced risk of infection, smaller stem cell harvest and improved effectiveness of genetically modified stem cells. The growth condition taught by Vavrova et al. are the same as to growth conditions disclosed in the instant specification (see Materials and Method and Table 3 in particular). It would be obvious to a person of ordinary skill in the art at the time the invention was made that the CD34+ HPC obtained and grown under the same conditions as disclosed in the instant specification would also be induced to differentiate into myeloid CD33+ cells with the same functional property as HPC recited in the instant claims absent a showing of unobvious property.